

**WHAT IS CLAIMED IS:**

1. A transdermal delivery device comprising:  
a drug containing layer comprising an effective amount of an opioid agonist and a plurality of microspheres dispersed in the drug containing layer, the microspheres comprising an opioid antagonist and being visually indiscernible in the drug containing layer.
2. The transdermal delivery device of claim 1, wherein the microspheres have a mean size of from about 1 to about 500  $\mu\text{m}$  in diameter.
3. A transdermal delivery device comprising:  
a drug containing layer comprising an effective amount of an opioid agonist and a plurality of microspheres dispersed in the drug containing layer, the microspheres comprising an opioid antagonist and in a mean size of from about 1 to about 500  $\mu\text{m}$  in diameter.
4. The transdermal delivery device of claim 3, wherein the microspheres are in a mean size of from about 1 to about 300  $\mu\text{m}$  in diameter.
5. The transdermal delivery device of claims 1 or 3, wherein the plurality of microspheres comprise the opioid antagonist dispersed in a polymeric matrix.
6. The transdermal delivery device of claims 1 or 3, wherein the microspheres further comprise a polymer selected from the group consisting of polyesters, polyethers, poly(orthoesters), polysaccharides, cyclodextrins, chitosans, poly ( $\Sigma$ -caprolactones), polyanhydrides, albumin, blends and copolymers thereof and mixtures thereof.
7. The transdermal delivery device of claims 1 or 3, wherein the microspheres consist essentially of the opioid antagonist and a polymer selected from the group consisting of polyesters, polyethers, poly(orthoesters), polysaccharides, cyclodextrins, chitosans, poly ( $\Sigma$ -caprolactones), polyanhydrides, albumin, blends

and copolymers thereof.

8. The transdermal delivery device of claims 1 or 3, wherein the microspheres consist essentially of the opioid antagonist dispersed in a polymeric matrix.
9. The transdermal delivery device of claims 1 or 3, wherein the microspheres are in a mean size of from about 300 to about 500 microns in diameter.
10. The transdermal delivery device of claims 1 or 3 , wherein the microspheres are in a mean size of from about 200 to about 500 microns in diameter.
11. The transdermal delivery device of claims 1 or 3, wherein the microspheres are in a mean size of from about 125 to about 200 microns in diameter.
12. The transdermal delivery device of claims 1 or 3, wherein the opioid antagonist becomes releasable if the transdermal delivery device is chewed, soaked, punctured, torn, or subjected to any other treatment which disrupts the integrity of the microspheres.
13. The transdermal delivery device of claims 1 or 3, wherein the effect of the opioid agonist is at least partially blocked when the delivery device is chewed, crushed or dissolved in a solvent, or subject to any other treatment which disrupts the integrity of the microspheres, and administered orally, intranasally, parenterally or sublingually.
14. The transdermal delivery device of claims 1 or 3, wherein the opioid antagonist is in the form of stable crystalline particles.
15. The transdermal delivery device of claims 1 or 3, wherein the microspheres are uniformly dispersed in within the drug layer.
16. The transdermal delivery device of claims 1 or 3, wherein the opioid agonist is selected from the group consisting of fentanyl, sufentanil, buprenorphine,

hydrocodone, morphine, hydromorphone, oxycodone, codeine, levorphanol, meperidine, methadone, oxymorphone, dihydrocodeine, tramadol, pharmaceutically acceptable salts thereof, and mixtures thereof.

17. The transdermal delivery device of claims 1, 3, or 16 wherein the opioid antagonist is selected from the group consisting of naltrexone, naloxone, nalmephene, diprenorphine, nalmexone, cyprenorphine, alazocine, oxilorphan, cyclophan, nalorphine, nalbuphine, buprenorphine butorphanol, cyclazocine, pentazocine, levallorphan, pharmaceutically acceptable salts thereof, and mixtures thereof.
18. The transdermal delivery device of claims 1 or 3, wherein the opioid antagonist is naltrexone or a pharmaceutically acceptable addition salt thereof.
19. The transdermal delivery device of claims 1 or 3, wherein the microspheres are in a mean size of from about 50 to about 100 microns in diameter.
20. The transdermal delivery device of claims 1 or 3, wherein the opioid analgesic is in an effective amount to provide analgesia for a period of time of from 2 to 8 days when affixed to the skin of the human patient.
21. The transdermal delivery device of claims 1 or 3, wherein the drug containing layer is a matrix layer.
22. The transdermal delivery device of claim 21, where the matrix comprises a material selected from the group consisting of polyethylene, polypropylene, ethylene/propylene copolymers, ethylene/ethylacrylate copolymers, ethylenevinyl acetate copolymers, silicones, rubber, rubber-like synthetic homo-, co- or block polymers, polyacrylic esters and the copolymers thereof, polyurethanes, polyisobutylene, chlorinated polyethylene, polyvinylchloride, vinyl chloride-vinyl acetate copolymer, polymethacrylate polymer (hydrogel), polyvinylidene chloride, poly(ethylene terephthalate), ethylene-vinyl alcohol copolymer, ethylene-vinyloxyethanol copolymer, silicones (e.g., silicone copolymers such as polysiloxane-polymethacrylate copolymers), cellulose polymers (e.g., ethyl

cellulose, and cellulose esters), polycarbonates, polytetrafluoroethylene and mixtures thereof.

23. The transdermal delivery device of claim 5, where the matrix is selected from the group consisting of silicone polymers, silicone polymers that are cross-linkable, copolymers having dimethyl and/or dimethylvinyl siloxane units which can be crosslinked, block copolymers based on styrene and 1,3-dienes, polyisobutylenes, polymers based on acrylate and/or methacrylate.
24. The transdermal delivery device of claim 21, further comprising an adhesive layer adjacent to, and in contact with, the matrix layer and permeable to the therapeutically active agent.
25. The transdermal delivery device of claims 1 or 3, wherein the drug containing layer is an adhesive layer.
26. The transdermal delivery device of claims 1 or 3, wherein the drug containing layer is a reservoir layer.
27. The transdermal delivery device of claim 26, further comprising a rate controlling membrane layer superimposed on the reservoir layer and substantially coextensive therewith.
28. The transdermal delivery device of claim 27, further comprising an adhesive layer adjacent to, and in contact with, the membrane layer and permeable to the therapeutically active agent.
29. The transdermal delivery device of claim 24, further comprising a protective layer covering and adhearing to the adhesive layer and removable therefrom for the use of the transdermal delivery device.
30. The transdermal delivery device of claims 1 or 3, wherein the transdermal delivery device is a device selected from the group consisting of a transdermal patch, a

transdermal plaster, a transdermal disc, and iontophoretic transdermal device.

31. The transdermal delivery device of claims 1 or 3, wherein the microspheres are in a mean size of from about 1 to about 200 microns in diameter.
32. The transdermal delivery device of claims 1 or 3, wherein the microspheres are in a mean size of from about 1 to about 100 microns in diameter.
33. The transdermal delivery device of claims 1 or 3, wherein the microspheres are in a mean size of from about 100 to about 500 microns in diameter.
34. A method of treating pain comprising applying a transdermal delivery device of claims 1 or 3 to the skin of a patient in need of pain relief.
35. A method of preventing abuse of an opioid agonist transdermal delivery device comprising making a transdermal delivery device of claims 1 or 3.
36. The use of the transdermal device of any claims 1-33, to provide analgesia to a patient in need thereof.